

**REMARKS**

Claims 1, 3-17, 29, and 31-55 were pending in the present application prior to this communication. By the present communication, claims 1, 9, 17 and 29 have been amended. New claims 56-78 have been added. No new matter is introduced by this amendment. Upon entry of the amendments submitted herewith, claims 1, 3-17, 29, 31-78 will be pending.

Support for amendments of claims 1, 9, 17, and 29 can be found throughout PCT/US98/13272A1 (WO99/00113), from which the instant application claims priority and incorporates by reference in its entirety. *See*, for example, page 36, line 15 to page 37, line 20 (describing a composition of protein-coated paclitaxel nanoparticles wherein the two components are unmodified paclitaxel and protein). A copy of the application is provided herein for the Examiner's convenience (See **Exhibit A**). Support for new claim 56 can be found in originally filed claim 16 of the present application. Support for new claims 57, 60, and 70 can be found, for example, at page 21, lines 22-24; page 22, lines 28-31 of PCT/US98/13272A1 (WO99/00113). Support for new claims 58, 61, and 71 can be found, for example, at page 36, lines 4-5 of PCT/US98/13272A1 (WO99/00113). Support for new claims 59, 63, and 72 can be found, for example, at page 22, lines 25 of PCT/US98/13272A1 (WO99/00113). Support for new claims 62 and 69 can be found, for example, in originally filed claim 7 of the present application. Support for claims 64-68 can be found, for example, in originally filed claims 10-14, respectively, of the present application. Support for new claims 73-76 can be found, for example, at page 7, line 5 and Examples 24 and 26 of the present application. Support for new claims 77 and 78 can be found, for example, at page 5, lines 25-30 and Example 26 of the present application.

The paragraph starting at page 1 of the specification following the section heading "RELATED APPLICATIONS" has been amended as indicated.

With respect to claim amendments and cancellation, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution

of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

### **Summary of the Interview**

Applicants thank the Examiner for the courtesy of telephonic interview on September 26, 2006, with inventor Neil Desai and Applicants' representatives Catherine Polizzi and Janet Xiao. The 35 U.S.C. § 103(a) rejection under Kunz et al. (U.S. Pat. No. 5,733,925) in view of Westesen et al. (U.S. Pat. No. 6,197,449) as well as the other § 103(a) rejections (which were directed to dependent claims) were discussed. Inventor and Applicants' representatives focused on the nature of the coating of nanoparticles used in the present invention and the differences between such nanoparticles and those taught in Kunz. Examiner suggested that independent claims (i.e., claims 1, 9, 17, and 29) be amended to recite "a coating consisting essentially of protein." Examiner's suggested claim amendment is reflected in this response.

### **Information Disclosure Statement**

An information disclosure statement will be filed after this response. The Examiner is respectfully requested to acknowledge receipt and review of the items provided with the information disclosure statement.

### **Withdrawn Rejections**

Applicants acknowledge with appreciation withdrawal of the 35 U.S.C. § 112, first paragraph rejection of claims 1, 3-18, and 20-30, as asserted in the Office Action mailed on July 15, 2005. Applicants acknowledge with appreciation withdrawal of the 35 U.S.C. § 102(e) rejection of claims 18, 20-28, and 30, and the 35 U.S.C. § 103(a) rejection of claims 1, 3-18, and 20-30, as asserted in the Office Action mailed on July 15, 2005. Applicants also acknowledge with appreciation withdrawal of the double patenting rejection of claims 18, 20-28, and 30, as asserted in the Office Action mailed on July 15, 2005.

**Rejection under 35 U.S.C. § 103(a) over Kunz et al. and Westesen et al.**

Claims 1, 3-17, 29, 31-33, 39-41, 47-49, and 55 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kunz et al. (U.S. Pat. No. 5,733,925, “Kunz”) and Westesen et al. (U.S. Pat. No. 6,197,449, “Westesen”). Applicants respectfully traverse.

To establish a *prima facie* case of obviousness, three criteria must be met. First, there must be some suggestion, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Third, there must be a reasonable expectation of success. MPEP §2143.

In an effort to expedite prosecution, all independent claims (i.e., claims 1, 9, 17, and 29) have been amended to recite a coating consisting essentially of protein, in accordance with the Examiner’s suggestion. The methods of the present invention (claims 1, 9, and 17) thus generally entail administering a composition comprising an amorphous drug in nanoparticle form, coated with a coating consisting essentially of protein, wherein said drug is selected from the group consisting of an antineoplastic, an antiproliferative, and angiogenesis inhibitor, and mixtures of any two or more thereof.<sup>1</sup> Kunz does not teach a composition comprising an amorphous drug in nanoparticle form, coated with a coating consisting essentially of protein.

Westesen is cited as allegedly providing motivation for utilizing amorphous forms of drugs. Westesen does not teach a composition comprising an amorphous drug in nanoparticle form, coated with a coating consisting essentially of protein. As explained in the previous response to Office Action, Westesen is directed to particles comprising a supercooled melt of a poorly soluble substance and a stabilizing agent. As readily recognizable by those skilled in the art and described in Westesen, to work with melts of a poorly soluble substance, one would, of necessity, have to work at temperatures sufficient to achieve a melt. See, for example, col. 15, line 15 (heating a

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<sup>1</sup> Claim 29 recites a method to reduce the toxicity of a drug that inhibits proliferation and migration of non-cancerous cells in a blood vessel, comprising combining said drug, in amorphous form and in the form of nanoparticles, with a biocompatible protein, wherein said drug is coated with a coating consisting essentially of said protein, wherein said drug is selected from the group consisting of an antineoplastic, an antiproliferative, an angiogenesis inhibitor, and mixtures of any two or more thereof.

mixture of a poorly water soluble substance and a stabilizing agent to 70°C); col. 19, line 24 (95°C); col. 22, line 8 (80°C). Such elevated temperatures would be incompatible with the structures of the nanoparticles used in the present invention. Accordingly, Applicants respectfully submit that Kunz and Westesen fail to teach all limitations in claims of the present application.

Furthermore, as discussed in the previous response to Office Action, the requisite elevated temperatures taught in Westesen would also be incompatible with the function of the proteins disclosed in Kunz. As a result, one would not be motivated to combine the teachings of Kunz and Westesen to arrive at methods of the present invention.

Accordingly, in view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

**Rejection under 35 U.S.C. § 103(a) over Kunz in view of Westesen, further in view of Mitragotri et al. and JP 05294839**

Claims 38, 46, and 54 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kunz in view of Westesen, further in view of Mitragotri et al. (U.S. Patent No. 5,814,599, “Mitragotri”) or JP 05294839. Applicants respectfully traverse.

Mitragotri and JP 05294839 are each cited as allegedly teaching the equivalency between particles made of polylactic acid, polyglycolic acid, and albumin. As discussed above, independent claims 1, 9, and 17 have been amended to recite a composition comprising an amorphous drug in nanoparticle form, coated with a coating consisting essentially of protein. Claims 38, 46, and 54 depend from claims 1, 9, and 17 respectively. As discussed above, neither Kunz nor Westesen teaches a composition comprising an amorphous drug in nanoparticle form, coated with a coating consisting essentially of protein.

Accordingly, in view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

**Rejection under 35 U.S.C. § 103(a) as being unpatentable over Kunz in view of Westesen further in view of Hunter**

Claims 34-35, 42-43, and 50-51 (all of which recite epothilone) are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kunz in view of Westesen, further in view of Hunter (U.S. Patent No. 5,994,341). Applicants respectfully traverse.

Hunter is cited as allegedly teaching that both epothilone and paclitaxel disrupt microtubule function. As discussed above, independent claims 1, 9, and 17 have been amended to recite a composition comprising an amorphous drug in nanoparticle form, coated with a coating consisting essentially of protein. Claims 34-35, 42-43, and 50-51 depend from claims 1, 9, and 17 respectively. As discussed above, neither Kunz nor Westesen teaches a composition comprising an amorphous drug in nanoparticle form, coated with a coating consisting essentially of protein.

Accordingly, in view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

**Rejection under 35 U.S.C. § 103(a) as being unpatentable over Kunz in view of Westesen, further in view of Marx**

Claims 36-37, 44-45, and 52-53 (all of which recite rapamycin) were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kunz in view of Westesen, further in view of Marx (Cir. Res. Vol. 76:412-417, 1995). Applicants respectfully traverse.

Marx is cited as allegedly teaching that rapamycin is an inhibitor of smooth muscle cells in the abnormal proliferation of restenosis. As discussed above, independent claims 1, 9, and 17 have been amended to recite a composition comprising an amorphous drug in nanoparticle form, coated with a coating consisting essentially of protein. Claims 36-37, 44-45, and 52-53 depend from claims 1, 9, and 17, respectively. As discussed above, neither Kunz nor Westesen teaches a composition comprising an amorphous drug in nanoparticle form, coated with a coating consisting essentially of protein.

Accordingly, in view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

### CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **420052000127**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

By   
Catherine M. Polizzi

Registration No.: 40,130  
MORRISON & FOERSTER LLP  
755 Page Mill Road  
Palo Alto, California 94304-1018  
(650) 813-5651